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PATENT  
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Assistant Commissioner for Patents  
Washington, D.C. 20231

August 9, 2002

TOWNSEND and TOWNSEND and CREW LLP

By:

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

John G.K. Williams *et al.*

Application No.: 09/876,374

Filed: June 6, 2001

For: CHARGE-SWITCH  
NUCLEOTIDES

Examiner: Lu, Frank

Art Unit: 1634

RESPONSE TO RESTRICTION  
REQUIREMENT

COPY OF PAPERS  
ORIGINALLY FILED

08/21/2002 SMINASS1 00000077 201430 09876374

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Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

In response to the Restriction Requirement mailed on July 12, 2002, please consider the following amendments remarks.

IN THE CLAIMS

Please add the following new claims 49-66.

1 49. (New) An intact charge-switch nucleotide phosphate (NP) probe,  
2 wherein, upon enzymatic cleavage of said intact charge-switch NP probe to produce a phosphate  
3 detectable moiety, said phosphate detectable moiety migrates to an electrode, and said intact  
4 charge-switch NP probe migrates to the other electrode.

1 50. (New) The intact charge-switch NP probe according to claim 49, wherein  
2 either said intact NP probe has a positive molecular charge, or wherein upon cleavage of said

3 phosphate detectable moiety, said phosphate detectable moiety carries a different charge relative  
4 to said intact NP probe.

1           **51.**     (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 either said intact NP probe has a negative molecular charge, or wherein upon cleavage of said  
3 phosphate detectable moiety, said phosphate detectable moiety carries a different charge relative  
4 to said intact NP probe.

1           **52.**     (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 said charge-switch NP probe is a nucleotide triphosphate (NTP); and wherein said phosphate  
3 detectable moiety is a pyrophosphate with a fluorophore moiety attached thereto.

1           **53.**     (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 said intact NTP probe has a positive charge.

A 1           **54.**     (New) The intact charge-switch NP probe according to claim **52**, wherein  
2 upon cleavage of said phosphate detectable moiety as a pyrophosphate fluorophore moiety, said  
3 pyrophosphate fluorophore moiety carries a positive charge relative to said intact NTP probe.

1           **55.**     (New) The intact charge-switch NP probe according to claim **52**, wherein  
2 upon cleavage of said phosphate detectable moiety as a pyrophosphate fluorophore moiety, said  
3 pyrophosphate fluorophore moiety carries a negative charge relative to said intact NTP probe.

1           **56.**     (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 said NTP probe is a member selected from the group consisting of a deoxynucleotide  
3 triphosphate (dNTP), and a nucleotide triphosphate (NTP).

1           **57.**     (New) The intact charge-switch NP probe according to claim **56**, wherein  
2 said NTP probe is a deoxynucleotide triphosphate (dNTP).

1           **58.**     (New) The intact charge-switch NP probe according to claim **57**, wherein  
2 said deoxynucleotide triphosphate (dNTP) is a member selected from the group consisting of

3 deoxyadenosine triphosphate, deoxycytosine triphosphate, deoxyguanosine triphosphate  
4 deoxythymidine triphosphate and deoxyuridine triphosphate.

1           **59.**   (New) The intact charge-switch NP probe according to claim **56**, wherein  
2 said nucleotide triphosphate (NTP) is a member selected from the group consisting of adenosine  
3 triphosphate, cytosine triphosphate, guanosine triphosphate and uridine triphosphate.

1           **60.**   (New) The intact charge-switch NP probe according to claim **52**, wherein  
2 said fluorophore moiety is attached to said terminal phosphate via a linker.

1           **61.**   (New) The intact charge-switch NP probe according to claim **60**, wherein  
2 said fluorophore linker is an alkylene group having between about 5 to about 12 carbons.

Al 1           **62.**   (New) The intact charge-switch NP probe according to claim **60**, wherein  
2 said linker carries at least one positive charge.

1           **63.**   (New) The intact charge-switch NP probe according to claim **60** wherein  
2 said linker carries at least two positive charges.

1           **64.**   (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 at least one of the phosphate moieties of said nucleotide phosphate probe has an ionized oxygen  
3 atom with a counter-cation associated therewith.

1           **65.**   (New) The intact charge-switch NP probe according to claim **49**, wherein  
2 said counter-cation is a metal ion.

1           **66.**   (New) The intact charge-switch NP probe according to claim **65**, wherein  
2 said metal ion is selected from the group consisting of  $Mg^{++}$ ,  $Mn^{++}$ ,  $K^{+}$  and  $Na^{+}$ .

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REMARKS

The Examiner has indicated that restriction to one of the following inventions  
is required under 35 U.S.C. § 121:

Group I. Claims 1-21, drawn to a charge-switch nucleotide phosphate probe.

Group II. Claims 22-34, drawn to a method for sequencing a labeled nucleotide phosphate having a detectable moiety from a released charged detectable moiety in a sample stream.

Group III. Claims 35 and 36, drawn to an analytical method for separating an intact NP probe.

Group IV. Claims 37-48, drawn to a method for sequencing a target nucleic acid with a polymerase.

Claims 1-66 are pending in this application and presented for examination.

Applicants hereby elect Group I, drawn to a charge-switch nucleotide phosphate probe, with traverse. Claims readable thereon include claims 1-21 and new claims 49-66. No new matter has been introduced with the newly added claims. Reconsideration is respectfully requested.

Claims 49-66 are newly added. Claim 49 sets forth an intact charge-switch nucleotide phosphate (NP) probe, wherein, upon enzymatic cleavage of the intact charge-switch NP probe to produce a phosphate detectable moiety, the phosphate detectable moiety migrates to an electrode, and the intact charge-switch NP probe migrates to the other electrode. Support for claim 49 is found throughout the specification as originally filed. More particularly, support is found on page 3, lines 30-32, bridging to page 4, lines 1-2.

Support for claims 50-59 is found, for example, in claims 2-9 as originally filed and page 12, lines 26-30. Support for claims 60-66 is found, for example, in claims 11-17. No new matter has been introduced, and therefore Applicants respectfully request that the Examiner enter the new claims.

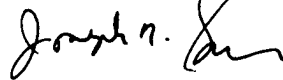
Applicants traversal is to the extent of rejoinder of the process claims after the product claims are found allowable. As the Examiner is aware, under M.P.E.P § 821.04, if

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Applicants elect claims directed to the product, and the product claims are allowable, withdrawn process claims which depend from or otherwise include all the limitations of the allowable product claims must be rejoined. Process claims, which depend from, or otherwise include all the limitations of the patentable product, will be entered as a matter of right. Therefore, upon allowance of the foregoing product claims, Applicant respectfully requests action on the merits of all process claims as well.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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